

Cheese articles	Appendix 1	Appendix 2	Sum of appendix 1 & 2	Tokyo R.	Uruguay R.	Grand total	Chapter 4/2010
EU-27 .....	2,417,127	964,873	3,382,000	.....	2,025,000	5,407,000	5,407,000
Romania .....	0	0	0	.....	500,000	500,000	500,000
Uruguay .....	0	0	0	428,000	750,000	1,178,000	1,178,000
Other Countries ....	0	13,064	13,064	.....	.....	13,064	13,064
SWISS OR EMMENTHALER CHEESE (NOTE 22)	5,182,610	1,468,704	6,651,314	823,519	380,000	7,854,833	7,854,833
EU-27 .....	3,918,461	1,233,533	5,151,994	393,006	380,000	5,925,000	5,925,000
Switzerland .....	1,230,651	188,836	1,419,487	430,513	.....	1,850,000	1,850,000
Other Countries ....	33,498	46,335	79,833	.....	.....	79,833	79,833
CHEESE AND SUBSTITUTES FOR CHEESE (NOTE 23)	1,837,206	2,587,702	4,424,908	1,050,000	0	5,474,908	5,474,908
EU-27 .....	1,837,206	2,587,701	4,424,907	.....	.....	4,424,907	4,424,907
Israel .....	0	0	0	50,000	.....	50,000	50,000
New Zealand .....	0	0	0	1,000,000	.....	1,000,000	1,000,000
Other Countries ....	0	1	1	.....	.....	1	1
SWISS OR EMMENTHALER CHEESE WITH EYE FORMATION (NOTE 25)	13,609,024	8,688,307	22,297,331	9,557,945	2,620,000	34,475,276	34,475,276
Argentina .....	0	9,115	9,115	70,885	.....	80,000	80,000
Australia .....	209,698	0	209,698	290,302	.....	500,000	500,000
Canada .....	0	0	0	70,000	.....	70,000	70,000
EU-27 .....	10,081,002	6,395,826	16,476,828	4,003,172	2,420,000	22,900,000	22,900,000
Iceland .....	0	149,999	149,999	150,001	.....	300,000	300,000
Israel .....	27,000	0	27,000	.....	.....	27,000	27,000
Norway .....	2,480,021	1,175,289	3,655,310	3,227,690	.....	6,883,000	6,883,000
Switzerland .....	763,050	921,055	1,684,105	1,745,895	200,000	3,630,000	3,630,000
Other Countries ....	48,253	37,023	85,276	.....	.....	85,276	85,276
TOTAL: CHEESE ARTICLES ..	55,069,411	32,831,232	87,900,643	22,764,145	24,921,000	135,585,788	135,585,788
TOTAL: CHEESE & NON-CHEESE ....	59,614,424	50,151,000	109,765,424	22,764,145	24,921,000	157,450,569	157,450,569

[FR Doc. 2015-19083 Filed 8-3-15; 8:45 am]

BILLING CODE 3410-10-P

**DEPARTMENT OF TRANSPORTATION**

**Federal Aviation Administration**

**14 CFR Part 39**

[Docket No. FAA-2015-3139; Directorate Identifier 2012-NM-139-AD; Amendment 39-18224; AD 2015-15-14]

RIN 2120-AA64

**Airworthiness Directives; BAE Systems (Operations) Limited Airplanes**

**AGENCY:** Federal Aviation Administration (FAA), Department of Transportation (DOT).

**ACTION:** Final rule; request for comments.

**SUMMARY:** We are adopting a new airworthiness directive (AD) for all BAE

Systems (Operations) Limited Model ATP airplanes. This AD requires a one-time inspection for solder deposited on the frangible plug of certain engine and auxiliary power unit (APU) fire extinguishers. This AD was prompted by reports of a fire extinguisher that failed to discharge due to solder deposited on the frangible plug of the fire extinguisher. We are issuing this AD to detect and correct solder deposited on the frangible plug of the fire extinguisher, which could result in failure of the fire extinguisher to discharge, and consequent inability to put out a fire in an engine or in the APU.

**DATES:** This AD becomes effective August 19, 2015.

The Director of the Federal Register approved the incorporation by reference of certain publications listed in this AD as of August 19, 2015.

We must receive comments on this AD by September 18, 2015.

**ADDRESSES:** You may send comments, using the procedures found in 14 CFR 11.43 and 11.45, by any of the following methods:

- *Federal eRulemaking Portal:* Go to <http://www.regulations.gov>. Follow the instructions for submitting comments.
- *Fax:* 202-493-2251.
- *Mail:* U.S. Department of Transportation, Docket Operations, M-30, West Building Ground Floor, Room W12-140, 1200 New Jersey Avenue SE., Washington, DC 20590.
- *Hand Delivery:* U.S. Department of Transportation, Docket Operations, M-30, West Building Ground Floor, Room W12-140, 1200 New Jersey Avenue SE., Washington, DC, between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays.

For BAE Systems (Operations) Limited service information identified in this AD, contact BAE Systems (Operations) Limited, Customer Information Department, Prestwick International Airport, Ayrshire, KA9 2RW, Scotland, United Kingdom;

telephone: +44 1292 675207; fax: +44 1292 675704; email: [RAPublications@baesystems.com](mailto:RAPublications@baesystems.com); Internet <http://www.baesystems.com/Businesses/RegionalAircraft/index.htm>.

For Kidde Graviner service information identified in this AD, contact Kidde Graviner Limited, Mathisen Way, Colnbrook, Slough, Berkshire, SL3 0HB, United Kingdom; telephone: +44 (0)1753 683245, fax: +44 (0)1753 685040.

You may view this referenced service information at the FAA, Transport Airplane Directorate, 1601 Lind Avenue SW., Renton, WA. For information on the availability of this material at the FAA, call 425-227-1221. It is also available on the Internet at <http://www.regulations.gov> by searching for and locating Docket No. FAA-2015-3139.

### Examining the AD Docket

You may examine the AD docket on the Internet at <http://www.regulations.gov> by searching for and locating Docket No. FAA-2015-3139; or in person at the Docket Operations office between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays. The AD docket contains this AD, the regulatory evaluation, any comments received, and other information. The street address for the Docket Operations office (telephone: 800-647-5527) is in the **ADDRESSES** section. Comments will be available in the AD docket shortly after receipt.

**FOR FURTHER INFORMATION CONTACT:** Todd Thompson, Aerospace Engineer, International Branch, ANM-116, Transport Airplane Directorate, FAA, 1601 Lind Avenue SW., Renton, WA 98057-3356; telephone: 425-227-1175; fax: 425-227-1149.

### SUPPLEMENTARY INFORMATION:

#### Discussion

The European Aviation Safety Agency (EASA), which is the Technical Agent for the Member States of the European Union, has issued EASA Airworthiness Directive 2012-0127R1, dated September 10, 2012 (referred to after this as the Mandatory Continuing Airworthiness Information, or "the MCAI"), to correct an unsafe condition for all BAE Systems (Operations) Limited Model ATP airplanes. The MCAI states:

A fire handle on a BAe 146 aeroplane was operated on the ground as a precautionary measure after the throttle cable on the affected engine failed, due to corrosion. The extinguisher failed to discharge.

Investigation results revealed that excess solder, which had been deposited during overhaul on the frangible plug of the

extinguisher, prevented the release of the extinguishant. Prompted by this report, Kidde Graviner, the fire extinguisher manufacturer, identified four further extinguishers of similar design that had the same issue. The ATP aeroplane extinguisher is one of those of a similar design.

This condition, if not detected and corrected, could result in the failure of a fire bottle to discharge, which reduces the ability of the fire protection system to extinguish fires in the engine or Auxiliary Power Unit (APU) fire zones, possibly resulting in damage to the aeroplane and injury to the occupants.

For the reasons described above, EASA issued AD 2012-0127 [dated July 10, 2012, <http://ad.easa.europa.eu/ad/2012-0127R1>] to require a one-time inspection of the affected Part Number (P/N) 57183 engine and APU fire extinguishers. In addition, this [EASA] AD prohibited installation of a fire extinguisher, unless it has passed the inspection as required by AD 2012-0127.

Revision 1 of this [EASA] AD is issued to clarify that new extinguishers P/N 57183 may be fitted with no additional inspection required by this [EASA] AD.

You may examine the MCAI on the Internet at <http://www.regulations.gov> by searching for and locating Docket No. FAA-2015-3139.

### Related Service Information Under 1 CFR Part 51

BAE Systems (Operations) Limited and Kidde Graviner have issued the following service information.

- BAE Systems (Operations) Limited Service Bulletin ATP-26-016, dated October 4, 2011. The service information describes procedures for an inspection for solder deposited on the frangible plug of certain engine and APU fire extinguishers.
- Kidde Graviner Service Bulletin 26-080, Revision 1, dated July 27, 2011. The service information describes procedures for an inspection for solder deposited on the frangible plug of certain engine and APU fire extinguishers.

This service information is reasonably available because the interested parties have access to it through their normal course of business or by the means identified in the **ADDRESSES** section of this AD.

### FAA's Determination and Requirements of This AD

This product has been approved by the aviation authority of another country, and is approved for operation in the United States. Pursuant to our bilateral agreement with the State of Design Authority, we have been notified of the unsafe condition described in the MCAI and service information referenced above. We are issuing this AD because we evaluated all pertinent

information and determined the unsafe condition exists and is likely to exist or develop on other products of the same type design.

### FAA's Determination of the Effective Date

Since there are currently no domestic operators of this product, notice and opportunity for public comment before issuing this AD are unnecessary.

### Comments Invited

This AD is a final rule that involves requirements affecting flight safety, and we did not precede it by notice and opportunity for public comment. We invite you to send any written relevant data, views, or arguments about this AD. Send your comments to an address listed under the **ADDRESSES** section. Include "Docket No. FAA-2015-3139; Directorate Identifier 2012-NM-139-AD" at the beginning of your comments. We specifically invite comments on the overall regulatory, economic, environmental, and energy aspects of this AD. We will consider all comments received by the closing date and may amend this AD based on those comments.

We will post all comments we receive, without change, to <http://www.regulations.gov>, including any personal information you provide. We will also post a report summarizing each substantive verbal contact we receive about this AD.

### Costs of Compliance

Currently, there are no affected airplanes on the U.S. Register. However, if an affected airplane is imported and placed on the U.S. Register in the future, the required actions will take about 1 work-hour, at an average labor rate of \$85 per work-hour. Based on these figures, we estimate the cost of this AD to be \$85 per airplane.

In addition, we estimate that any necessary follow-on actions will take about 1 work-hour and require parts costing \$7,042, for a cost of \$7,127 per product.

### Authority for This Rulemaking

Title 49 of the United States Code specifies the FAA's authority to issue rules on aviation safety. Subtitle I, section 106, describes the authority of the FAA Administrator. "Subtitle VII: Aviation Programs," describes in more detail the scope of the Agency's authority.

We are issuing this rulemaking under the authority described in "Subtitle VII, Part A, Subpart III, Section 44701: General requirements." Under that section, Congress charges the FAA with

promoting safe flight of civil aircraft in air commerce by prescribing regulations for practices, methods, and procedures the Administrator finds necessary for safety in air commerce. This regulation is within the scope of that authority because it addresses an unsafe condition that is likely to exist or develop on products identified in this rulemaking action.

### Regulatory Findings

We determined that this AD will not have federalism implications under Executive Order 13132. This AD will not have a substantial direct effect on the 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.

For the reasons discussed above, I certify that this AD:

1. Is not a "significant regulatory action" under Executive Order 12866;
2. Is not a "significant rule" under the DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979);
3. Will not affect intrastate aviation in Alaska; and
4. Will not have a significant economic impact, positive or negative, on a substantial number of small entities under the criteria of the Regulatory Flexibility Act.

### List of Subjects in 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Incorporation by reference, Safety.

### Adoption of the Amendment

Accordingly, under the authority delegated to me by the Administrator, the FAA amends 14 CFR part 39 as follows:

## PART 39—AIRWORTHINESS DIRECTIVES

- 1. The authority citation for part 39 continues to read as follows:

**Authority:** 49 U.S.C. 106(g), 40113, 44701.

### § 39.13 [Amended]

- 2. The FAA amends § 39.13 by adding the following new airworthiness directive (AD):

#### 2015-15-14 BAE Systems (Operations)

**Limited:** Amendment 39-18224. Docket No. FAA-2015-3139; Directorate Identifier 2012-NM-139-AD.

#### (a) Effective Date

This AD becomes effective August 19, 2015.

#### (b) Affected ADs

None.

#### (c) Applicability

This AD applies to all BAE Systems (Operations) Limited Model ATP airplanes, certificated in any category, all manufacturer serial numbers.

#### (d) Subject

Air Transport Association (ATA) of America Code 26, Fire Protection.

#### (e) Reason

This AD was prompted by reports of a fire extinguisher that failed to discharge due to solder deposited on the frangible plug of the fire extinguisher. We are issuing this AD to detect and correct solder deposited on the frangible plug of the fire extinguisher, which could result in failure of the fire extinguisher to discharge, and consequent inability to put out a fire in an engine or in the APU.

#### (f) Compliance

Comply with this AD within the compliance times specified, unless already done.

#### (g) Inspection of Fire Extinguishers

(1) For airplanes equipped with Kidde Graviner fire extinguishers having part number (P/N) 57183 (all dash numbers): Within 12 months after the effective date of this AD, inspect each affected fire extinguisher for solder deposited on the frangible plug of the fire extinguisher, in accordance with the Accomplishment Instructions of BAE Systems (Operations) Limited Service Bulletin ATP-26-016, dated October 4, 2011, and Kidde Graviner Service Bulletin 26-080, Revision 1, dated July 27, 2011. If any solder deposit is detected, replace the fire extinguisher with a serviceable fire extinguisher before further flight, in accordance with the Accomplishment Instructions of BAE Systems (Operations) Limited Service Bulletin ATP-26-016, dated October 4, 2011.

(2) Fire extinguishers that meet any condition identified in paragraph (g)(2)(i), (g)(2)(ii), or (g)(2)(iii) of this AD are compliant with the requirements of paragraph (g)(1) of this AD.

(i) Fire extinguishers that have been overhauled by Kidde Graviner or Hugen.

(ii) Fire extinguishers that have been overhauled as specified in Kidde Graviner Service Information Letter (SIL) 01-10, dated July 29, 2010.

(iii) Fire extinguishers that have been overhauled as specified in Kidde Graviner Component Maintenance Manual with Illustrated Parts List 26-21-52, Automatic Extinguishers with Steel Containers Part Numbers 57133, 57135, 57145, and 57183 Series, Revision 17, dated June 13, 2012.

#### (h) Definition of "Overhaul"

For the purpose of this AD, an overhaul is considered to include replacement of the operating head. Replacement of the pressure relief plug assembly only is not considered an overhaul.

#### (i) Parts Installation Limitations

As of the effective date of this AD, do not install a Kidde Graviner fire extinguisher having P/N 57183 (all dash numbers) on any airplane, unless the fire extinguisher meets

any condition specified in paragraph (i)(1), (i)(2), (i)(3), (i)(4), or (i)(5) of this AD.

(1) The fire extinguisher is new.

(2) The fire extinguisher has passed the inspection as specified in the instructions of Kidde Graviner Service Bulletin 26-080, Revision 1, dated July 27, 2011.

(3) The fire extinguisher has been overhauled by Kidde Graviner or Hugen.

(4) The fire extinguisher has been overhauled as specified in the instructions of Kidde Graviner SIL 01-10, dated July 29, 2010.

(5) The fire extinguisher has been overhauled in accordance with Kidde Graviner Component Maintenance Manual with Illustrated Parts List 26-21-52, Automatic Extinguishers with Steel Containers Part Numbers 57133, 57135, 57145, and 57183 Series, Revision 17, dated June 13, 2012.

#### (j) Credit for Previous Actions

This paragraph provides credit for the actions specified in paragraphs (g)(2)(iii) and (i)(5) of this AD, if those actions were performed before the effective date of this AD in accordance with the service information identified in paragraph (j)(1), (j)(2), (j)(3), or (j)(4) of this AD. These documents are not incorporated by reference in this AD.

(1) Kidde Graviner Component Maintenance Manual with Illustrated Parts List 26-21-52, Automatic Extinguishers with Steel Containers Part Numbers 57133, 57135, 57145, and 57183 Series, Revision 13, dated August 9, 2010.

(2) Kidde Graviner Component Maintenance Manual with Illustrated Parts List 26-21-52, Automatic Extinguishers with Steel Containers Part Numbers 57133, 57135, 57145, and 57183 Series, Revision 14, dated August 8, 2011.

(3) Kidde Graviner Component Maintenance Manual with Illustrated Parts List 26-21-52, Automatic Extinguishers with Steel Containers Part Numbers 57133, 57135, 57145, and 57183 Series, Revision 15, dated January 16, 2012.

(4) Kidde Graviner Component Maintenance Manual with Illustrated Parts List 26-21-52, Automatic Extinguishers with Steel Containers Part Numbers 57133, 57135, 57145, and 57183 Series, Revision 16, dated May 21, 2012.

#### (k) Other FAA AD Provisions

The following provisions also apply to this AD:

(1) *Alternative Methods of Compliance (AMOCs):* The Manager, International Branch, ANM-116, Transport Airplane Directorate, FAA, has the authority to approve AMOCs for this AD, if requested using the procedures found in 14 CFR 39.19. In accordance with 14 CFR 39.19, send your request to your principal inspector or local Flight Standards District Office, as appropriate. If sending information directly to the International Branch, send it to ATTN: Todd Thompson, Aerospace Engineer, International Branch, ANM-116, Transport Airplane Directorate, FAA, 1601 Lind Avenue SW., Renton, WA 98057-3356; telephone 425-227-1175; fax 425-227-1149. Information may be emailed to: 9-ANM-116-

AMOC-REQUESTS@faa.gov. Before using any approved AMOC, notify your appropriate principal inspector, or lacking a principal inspector, the manager of the local flight standards district office/certificate holding district office. The AMOC approval letter must specifically reference this AD.

(2) *Contacting the Manufacturer:* For any requirement in this AD to obtain corrective actions from a manufacturer, the action must be accomplished using a method approved by the Manager, International Branch, ANM-116, Transport Airplane Directorate, FAA; or the European Aviation Safety Agency (EASA); or BAE Systems (Operations) Limited's EASA Design Organization Approval (DOA). If approved by the DOA, the approval must include the DOA-authorized signature.

#### (l) Related Information

(1) Refer to Mandatory Continuing Airworthiness Information (MCAI) EASA Airworthiness Directive 2012-0127R1, dated September 10, 2012, for related information. You may examine the MCAI on the Internet at <http://www.regulations.gov> by searching for and locating Docket No. FAA-2015-3139.

(2) Service information identified in this AD that is not incorporated by reference is available at the addresses specified in paragraphs (m)(4), (m)(5), and (m)(6) of this AD.

#### (m) Material Incorporated by Reference

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

(2) You must use this service information as applicable to do the actions required by this AD, unless this AD specifies otherwise.

(i) BAE Systems (Operations) Limited Service Bulletin ATP-26-016, dated October 4, 2011.

(ii) Kidde Graviner Service Bulletin 26-080, Revision 1, dated July 27, 2011.

(3) For BAE Systems (Operations) Limited service information identified in this AD, contact BAE Systems (Operations) Limited, Customer Information Department, Prestwick International Airport, Ayrshire, KA9 2RW, Scotland, United Kingdom; telephone +44 1292 675207; fax +44 1292 675704; email [RApublications@baesystems.com](mailto:RApublications@baesystems.com); Internet <http://www.baesystems.com/Businesses/RegionalAircraft/index.htm>.

(4) For Kidde Graviner service information identified in this AD, contact Kidde Graviner Limited, Mathisen Way, Colnbrook, Slough, Berkshire, SL3 0HB, United Kingdom; Telephone: +44 (0)1753 683245, Fax: +44 (0)1753 685040.

(5) You may view this service information at the FAA, Transport Airplane Directorate, 1601 Lind Avenue SW., Renton, WA. For information on the availability of this material at the FAA, call 425-227-1221.

(6) You may view this service information that is incorporated by reference 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 July 23, 2015.

**Victor Wicklund,**

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

[FR Doc. 2015-18710 Filed 8-3-15; 8:45 am]

**BILLING CODE 4910-13-P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### 21 CFR Part 73

[Docket Nos. FDA-2014-C-1616 and FDA-2015-C-0245]

#### Listing of Color Additives Exempt From Certification; Mica-Based Pearlescent Pigments; Confirmation of Effective Date

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

**ACTION:** Final rule; confirmation of effective date.

**SUMMARY:** The Food and Drug Administration (FDA or we) is confirming the effective date of July 9, 2015, for the final rule that appeared in the **Federal Register** of June 8, 2015, and that amended the color additive regulations to expand the permitted uses of mica-based pearlescent pigments prepared from titanium dioxide and mica as color additives in cordials, liqueurs, flavored alcoholic malt beverages, wine coolers, cocktails, non-alcoholic cocktail mixers and mixes, and in egg decorating kits for coloring shell eggs.

**DATES:** Effective date of final rule published in the **Federal Register** of June 8, 2015 (80 FR 32303), confirmed: July 9, 2015.

**FOR FURTHER INFORMATION CONTACT:** Ellen Anderson, Center for Food Safety and Applied Nutrition (HFS-265), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740-3835, 240-402-1309.

**SUPPLEMENTARY INFORMATION:** In the **Federal Register** of June 8, 2015 (80 FR 32303), we amended the color additive regulations in § 73.350 *Mica-based pearlescent pigments* (21 CFR 73.350) to expand the permitted uses of mica-based pearlescent pigments prepared from titanium dioxide and mica as color additives in cordials, liqueurs, flavored alcoholic malt beverages, wine coolers, cocktails, non-alcoholic cocktail mixers and mixes, and in egg decorating kits for coloring shell eggs.

We gave interested persons until July 8, 2015, to file objections or requests for

a hearing. We received no objections or requests for a hearing on the final rule. Therefore, we find that the effective date of the final rule that published in the **Federal Register** of June 8, 2015, should be confirmed.

#### List of Subjects in 21 CFR Part 73

Color additives, Cosmetics, Drugs, Foods, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 341, 342, 343, 348, 351, 352, 355, 361, 362, 371, 379e) and under authority delegated to the Commissioner of Food and Drugs, and redelegated to the Director, Office of Food Additive Safety, we are giving notice that no objections or requests for a hearing were filed in response to the June 8, 2015, final rule. Accordingly, the amendments issued thereby became effective July 9, 2015.

Dated: July 29, 2015.

**Susan Bernard,**

*Director, Office of Regulations, Policy and Social Sciences, Center for Food Safety and Applied Nutrition.*

[FR Doc. 2015-18996 Filed 8-3-15; 8:45 am]

**BILLING CODE 4164-01-P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### 21 CFR Part 866

[Docket No. FDA-2015-N-2526]

#### Medical Devices; Immunology and Microbiology Devices; Classification of *Trichomonas Vaginalis* Nucleic Acid Assay

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

**ACTION:** Final order.

**SUMMARY:** The Food and Drug Administration (FDA) is classifying a *Trichomonas vaginalis* nucleic acid assay into class II (special controls). The Agency is classifying the device into class II (special controls) in order to provide a reasonable assurance of safety and effectiveness of the device.

**DATES:** This order is effective August 4, 2015. The classification was applicable April 19, 2011.

**FOR FURTHER INFORMATION CONTACT:** Himani Bisht, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5565, Silver Spring, MD 20993-0002, 301-796-6189.

**SUPPLEMENTARY INFORMATION:**